

From Bench to Battlefield: The Neuroscience of Combat Stress Risk and Resilience

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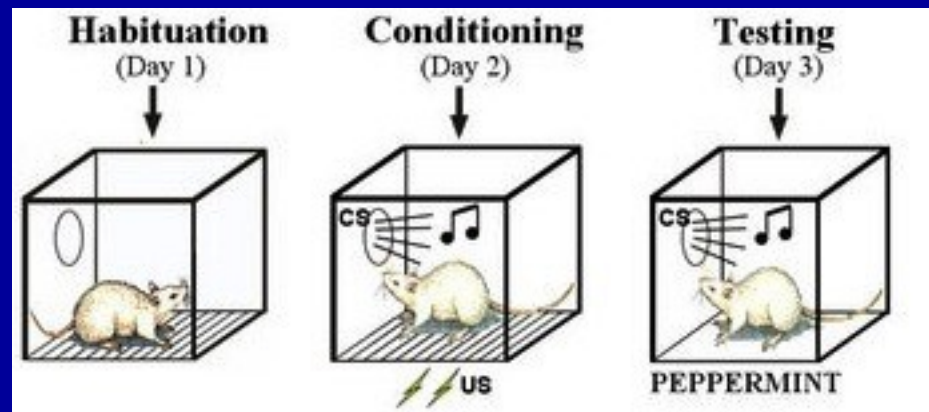
Objectives

- Describe how neuroscience research methods help us better define combat stress
 - Risk
 - Resilience
- Translate neuroscience research methods into clinical practice/operations.

What is “normal” stress response?

- OIF/OEF PTSD risk is 1 in 5.
- A monozygotic twin makes risk 1 in 3.
- Civilian research focused on illness risk
- We need to better understand:
 - Resistance: same stress exposure, no illness
 - Resilience: faster recovery from illness
- What can neurobiology of fear tell us?

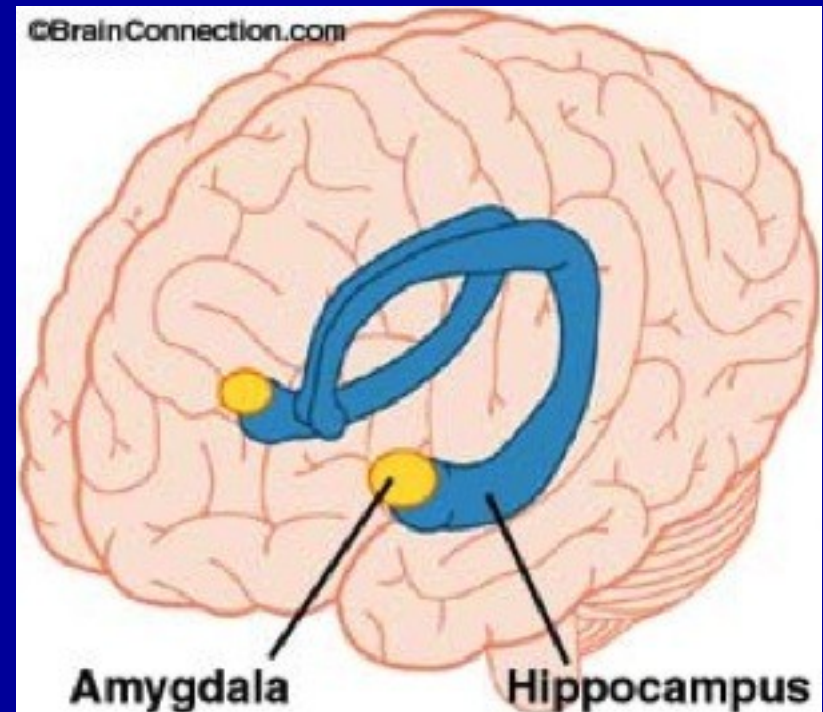
Biobehavioral model of fear



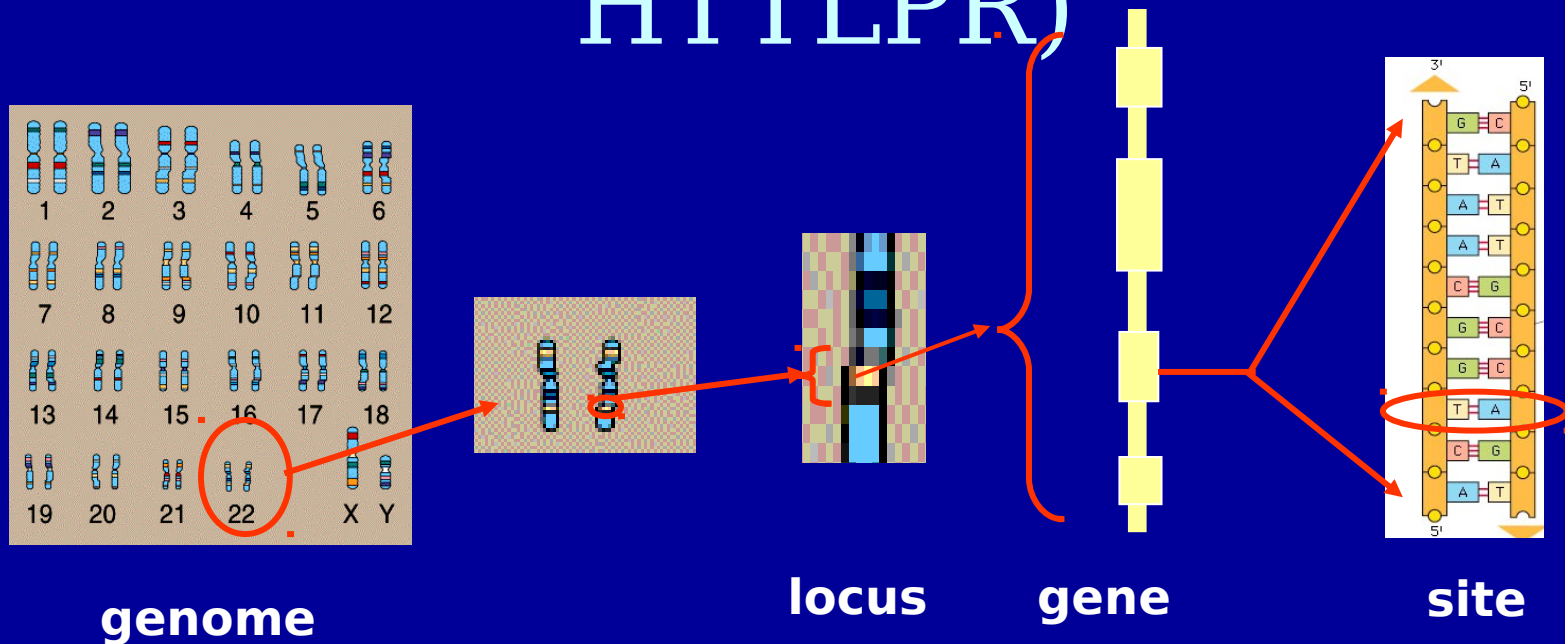
- PTSD thought of in terms of Pavlovian conditioning:
 - An over-reaction to threat cue.
 - This model used to develop new drug trials.
 - Yet, only one of six PTSD studies support this model.
 - Why so much variance in PTSD fear learning ability?

Neurobiology of Fear

- Conditioned fear ability associated with amygdala brain region
- Amygdala activity regulated in part by serotonin neurotransmitter.
- Serotonin affects depression and anxiety.



Serotonin Transporter Promoter Variant (5-HTTLPR)



**Pair of
Chromosomes
(2 Strands of DNA
each)**

- Common polymorphism in promoter region regulates gene expression
- Genotypes: l/l or l/s or s/s
- Long variant = increased serotonin “RESILIENCE”

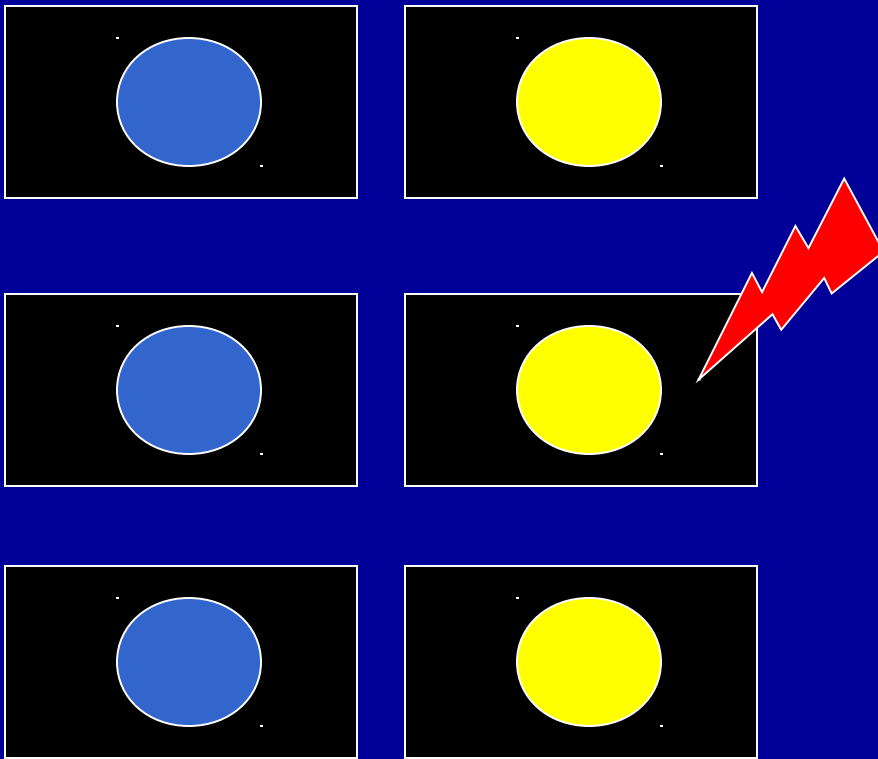
Current Study

- Investigate ability to learn fear and safety cues
- Compare PTSD and Stress Resistant Service Members
- Study brain activity during fear learning
- Categorize Service Members by Serotonin risk and resilience gene variants.

Participants

- 10th Mountain Division (LI).
 - Right handed, medication-free, metal-free.
- Active Duty Male Service Members:
 - PTSD (n=14).
 - Combat Resilient (n=14).
 - Pre-Deployed (n=15).

Research Procedure



Demographics

	PTSD	Stress Resistant
Age	24 (3)	24 (3)
Education	12 (1)	13 (1)
Yrs. Service	4 (3)	5 (2)
CES	30 (7)	27 (6)
CAPS	66 (4)	16 (4)

Identifying Threat (CS+) from Safety (CS-)

The ability to discriminate threat from safety varies by 5HT2C polymorphism

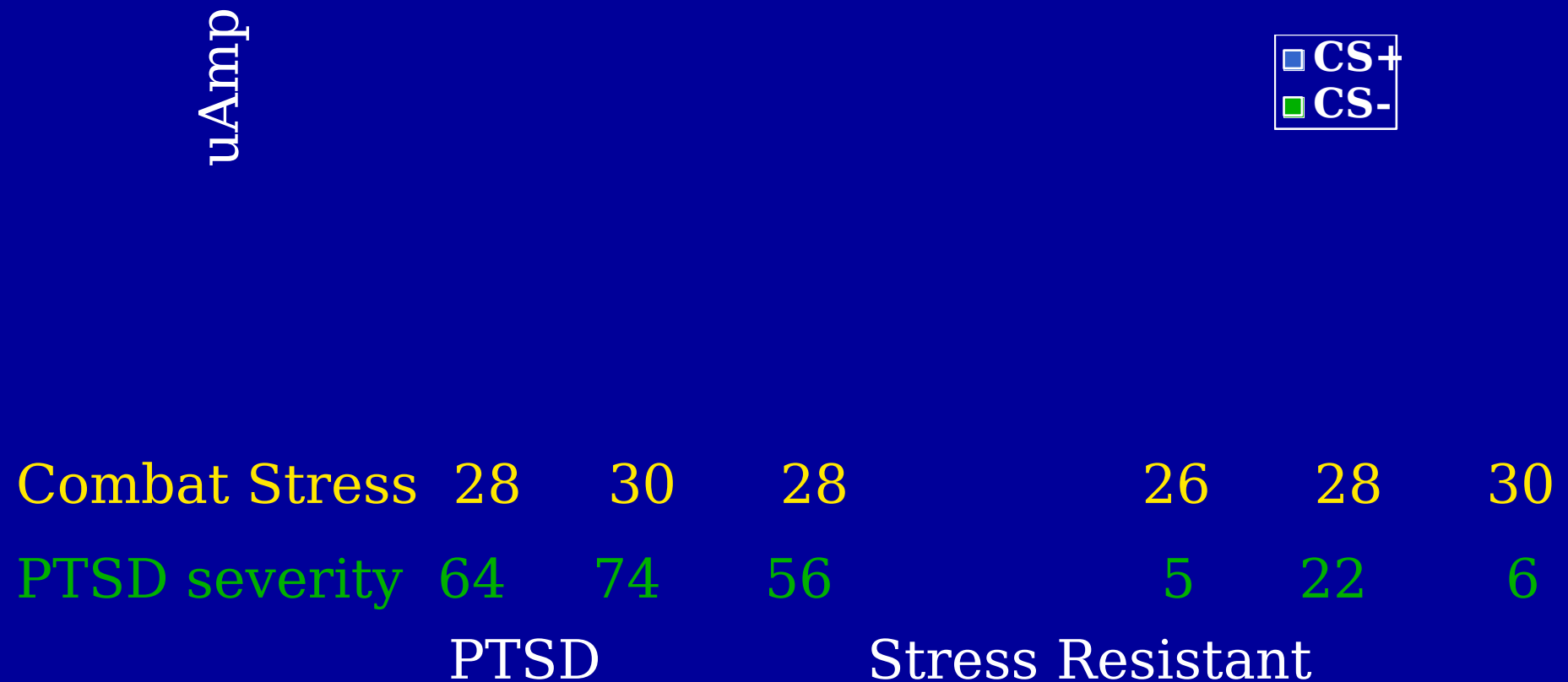
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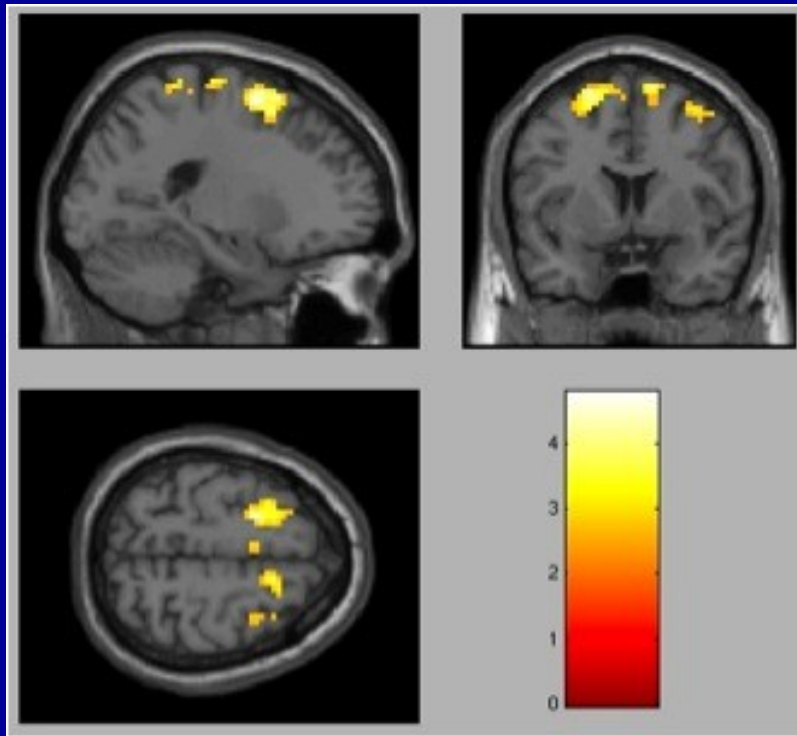
PTSD

Stress Resistant

The ability to discriminate threat from safety varies by 5HT2C polymorphism



fMRI Results: Stress Resistant



Stress Resistant Service Members show greater CR+ in Lateral

BA6 is defined as a pre-motor area, often found active during cognitive tasks to prepare for action.

Activity motor areas may inhibit activity in fear network.

Summary: PTSD

- No support for “over reaction” model.
 - Over time, a “general alarm”
- “Risk” gene associated increased PTSD severity and poor ability to identify threat from safety signals.

Summary: Stress Resistance

- Stress Resistant Service Members not “fearless”.
- Make good use of threat and safety cues.
 - Conditioned fear response engages brain areas for motor output planning.
 - Likely prevents fear circuit from over-reacting.
- Provide building blocks for operational functioning.

Translation to Clinical Value

- In separate pilot study:
 - Veterans with strong conditioned response responded very well to 8 wk SNRI treatment (Duloxetine).
 - Veterans with weak/no conditioned response saw no improvement.
- Conditioned Fear provides marker for treatment.
- Need to change models for treatment.
- Can we screen for stress resistant Service Members?

Research Team

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